Assignment 05

PUBH 8878

Setup

```r
set.seed(8878)

library(ggplot2)
library(dplyr)
library(tibble)
```

Data for the assignment

We simulate m test statistics using the two-groups model discussed in lecture, then convert to two-sided p-values.

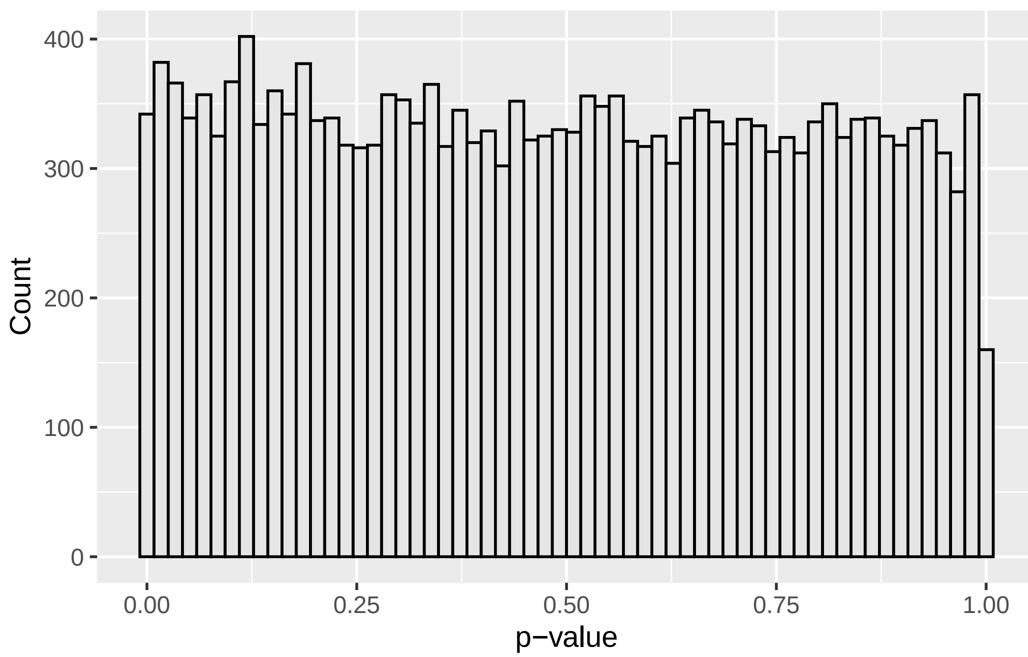
```r
m <- 20000
pi0_true   <- 0.95 # fraction of nulls
sigma_true <- 2.0 # sd under alternative
tau_true   <- 1.0 # sd under null (standard normal null)

H <- rbinom(m, 1, 1 - pi0_true) # 1 = non-null, 0 = null
z <- numeric(m)
z[H == 0] <- rnorm(sum(H == 0), 0, tau_true) # null z
z[H == 1] <- rnorm(sum(H == 1), 0, sigma_true) # alt z
p <- 2 * pnorm(-abs(z)) # two-sided p-values

dat <- tibble(i = seq_len(m), z = z, p = p, H = H)
```

A quick look:

```r
dat |> summarize(
  m      = n(),
  m0     = sum(H == 0),
  m1     = sum(H == 1),
  pi0    = mean(H == 0),
  min_p  = min(p),
  med_p  = median(p)
) |>
  kableExtra::kable(digits = 3)
```

m	m0	m1	pi0	min_p	med_p
20000	19010	990	0.951	0	0.486

```r
ggplot(dat, aes(p)) +
  geom_histogram(bins = 60, color = "black", fill = "grey90") +
  labs(x = "p-value", y = "Count")
```



Problem 1: Some theory (20 pts)

(a) (4 pts) Prove that if a continuous test statistic T has null cdf F_0, then the one-sided p-value $P = 1 - F_0(T)$ is **Uniform(0,1)** under the null. (Hint: use the probability integral transform.)

(b) Show that $\mathrm{BFDR}(A) = \frac{F_0(A)\pi_0}{F(A)}$. Then, let $\mathrm{lfdr}(z) = \Pr(H = 0 \mid Z = z) = \frac{\pi_0 f_0(z)}{f(z)}$. Prove the averaging identity $\mathrm{BFDR}(A) = \mathbb{E}[\,\mathrm{lfdr}(Z) \mid Z \in A\,]$. (Hint: write both numerator and denominator as integrals over A.)

(c) (3 pts) Briefly describe the key difference between *FDR control at level q* (e.g., BH) and reporting local false discovery rates (lfdr) for individual hypotheses.

Problem 2: Implement BH step-up from scratch (20 pts)

We will implement the BH decision rule and compare to built-ins.

(a) (10 pts) Write an R function `bh_from_scratch(p, q)` that:

1. orders the input vector of p-values `p`
2. finds $k = \max\{i : \; p_{(i)} \le (i/m)q\}$ (take $k = 0$ if the set is empty)
3. returns a list with `$k`, the BH threshold $\alpha^* = (k/m)q$, and a logical vector `reject` of length `m` marking rejections.

Then run it at `q = 0.10` on the vector `dat$p`. Produce a plot overlaying the ordered `p_(i)` and the BH line $(i/m)q$, and mark the chosen cutoff.

(b) (5 pts) Compare your rejections to `p.adjust(dat$p, method="BH") <= 0.10`. They should match exactly. Report the number of discoveries.

(c) (5 pts) Report the *empirical FDP* on this simulated data, $Q = V/\max(1, R)$, using the latent truth `H` (remember: `H==0` means null). Comment briefly.

Problem 3: Simulation study of BH FDR control (20 pts)

Design a small simulation to assess how the BH FDR behaves as a function of π_0 and the alternative strength.

- Fix `m = 5000`, `q = 0.10`. For each $\pi_0 \in \{0.6, 0.8, 0.9, 0.95\}$ and alternative sd $\sigma \in \{1.5, 2.0\}$:
  - simulate 200 independent datasets via the two-groups model with `tau = 1`,
  - apply BH at level `q`,
  - record the FDP for each replication using the latent truth.
- Plot the average FDP and its simulation SE versus π_0 for each σ. Does BH control FDR near $\pi_0 q$ under independence?

Problem 4: Empirical-Bayes BFDR from p-values (20 pts)

We will estimate the Bayesian FDR at a threshold p_t using

$$\widehat{\mathrm{BFDR}}(p_t) = \frac{\hat{\pi}_0 \, p_t}{\hat{F}(p_t)}, \qquad \hat{F}(p_t) = \frac{1}{m} \sum_{i=1}^{m} \mathbf{1}\{p_i \le p_t\}.$$

(a) (8 pts) Implement the Storey (2002) estimator

$$\hat{\pi}_0(\lambda) = \frac{\#\{p_i > \lambda\}}{m(1-\lambda)}, \qquad \lambda \in [0.5, 0.95],$$

and report the smoothed estimate $\hat{\pi}_0$ obtained by fitting a cubic spline or loess of $\hat{\pi}_0(\lambda)$ versus λ and evaluating at $\lambda = 1$

(b) (6 pts) For a grid of thresholds $p_t \in \{10^{-6}, 10^{-5}, \ldots, 10^{-1}\}$, compute $\widehat{\mathrm{BFDR}}(p_t)$ and plot it as a function of p_t.

(c) (6 pts) Pick the smallest p_t whose estimated BFDR is ≤ 0.10 and report how many discoveries you would make at that threshold. Compare to the BH discoveries at $q = 0.10$ from Problem 2.

Compare your $\hat{\pi}_0$ to the estimate from the `qvalue` package and report both.

Problem 5: q-values and discovery sets (10 pts)

Compute `qvalues <- qvalue::qvalue(dat$p)` and:

(a) (4 pts) Report how many features have `qvalues$qvalues <= 0.10`. Compare to BH at $q = 0.10$ and to your BFDR-based threshold in Problem 4.

(b) (6 pts) Sort features by their q-values (ascending). Let $\bar{q}(k)$ be the running mean of the first k q-values. Plot $\bar{q}(k)$ versus k and mark the largest $\hat{k}$ with $\bar{q}(\hat{k}) \le 0.10$. Explain why selecting the first $\hat{k}$ features is a reasonable discovery rule.

Problem 6: Brief discussion (20 pts)

Write a concise paragraph (6–10 sentences) addressing the following:

- How do BH, BFDR thresholding, and q-value selection compare on these data in terms of number of discoveries and estimated error rates?
- What assumptions underlie BH control, and how might LD (dependence among tests) in GWAS affect it?
- What are potential pitfalls of estimating π_0 from the empirical distribution of p-values?